

VA



U.S. Department
of Veterans Affairs

Research Advisory Committee on Gulf War Veterans' illnesses (RACGWVI)

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Designated Federal Officer (DFO)
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Washington D.C.



Research Advisory Committee on Gulf War Veterans' illnesses: Overview

The Research Advisory Committee on Gulf War Veterans' Illnesses was created by Congress in 1998, and first appointed by Secretary of Veterans Affairs in January 2002.

Mission

The Research Advisory Committee on Gulf War Veterans' Illnesses provides advice and makes recommendations to the Secretary of Veterans Affairs on proposed research studies, plans, and strategies related to understanding and treating the health consequences of military service in the Southwest Asia theater of operations during the 1990 - 91 Gulf War.

- Welcome to our first in person meeting since October 2019.
- The VA Advisory Committee Handbook has been provided, if you need another copy, let us know.
- Annual Requirements: FACA 101 and Ethics Training and Special Government Employee (SGE) Self-Certification.



FY22 - RACGWVI Recommendations (1 OF 4)

RECOMMENDATION 1: Fund research into key focus areas, examples below, to support the diagnosis and treatment of GWI.

- Basic and clinical studies on the role of the microbiome in the etiology and maintenance of GWI.
- Basic and clinical studies to determine the effects of dietary manipulations on the quality of life for GWV with GWI. Examples include low-glutamate and low Fermentable Oligosaccharides, Disaccharides, Monosaccharides And Polyols (FODMAP) diets used clinically to reduce gastrointestinal and other symptoms.
- Basic and clinical studies to further evaluate the status and/or influence of mitochondrial function in GWV, with and without, GWI.
- Determine the utility of the Department of Defense Serum Repository as a resource for investigators studying GWI. Among other utilities, the repository's samples may be useful in confirming a correlation between butyrylcholinesterase inhibition (itself and as a biomarker of acetylcholinesterase) and pyridostigmine bromide exposures as potential sources which cause GWI.
- Conduct a prospective, double-blind randomized clinical trial to determine the effects of antioxidants, ubiquinol vs ubiquinone, on the quality of life for GWV with GWI.



FY22 - RACGWVI Recommendations (1 OF 4)

VA RESPONSE

VARESPONSE (*CONCUR*).

Promising VA- and non-VA funded research in progress and close to implementation were highlighted at the 2020 VA:DoD State-of-the-Science Meeting and during FY21 Committee meetings. Collaborations have been discussed and are encouraged.

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FY22 - RACGWVI Recommendations (2 OF 4)

RECOMMENDATION 2: Establish one or more Gulf War-Military Exposure Research Innovation Center(s) (GW-MERIC). The RACGWVI recommends that VA Office of Research and Development (ORD) establish one or more GW-MERIC(s) with a two-part mission: 1) To expedite and implement evidence-based clinical treatment and diagnostic research for GWV with GWI, and 2) Build upon existing collaborations and establish new VA and non-VA partnerships to leverage and expand subject matter expertise, data and specimen resources, and technology.

GW-MERIC projects should include diverse team-based approaches through supporting multi-investigator, multi-institution partnerships and recruiting new and junior investigators into the field to advance translation of research. The GW-MERIC(s) would coordinate a strategic approach supporting GWI-focused, program-directed projects and a learning healthcare system model to integrate research into clinical care.



FY22 - RACGWVI Recommendations (2 OF 4)

VA RESPONSE

VA RESPONSE (CONCUR).

This recommendation builds on the VA Secretary's top to bottom review on how the VA can improve the system assessing the health outcomes of military exposures and his primary messages including 1) improving science, surveillance, epidemiology and research to inform decisions grounded in science and 2) providing expanded training for health care providers.

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FY22 - RACGWVI Recommendations (2 OF 4)

ORD ACTION

Gulf War Implementation MERIC. Accelerating the translation of research and evidence-based practices into care.



MERIC PI:
Lisa McAndrew, PhD



MERIC PI:
Stephen Hunt, MD

Project-1 Lead:

Shannon Nugent, PhD

Project-2 Lead:

April Mohanty, PhD, MPH

Project-3 Lead:

Autumn Gallegos, PhD

Project-4 Lead:

*Lisa M. McAndrew,
Ph.D.*

Operational Partners:

Tom Mattras, Director of Primary Care Operations

Benjamin Kligler, Executive Director of Patient Centered Care and Cultural Transformation

Kelly Howard, Whole Health National Education, Program Lead

Patricia Hastings, Chief Consultant, Health Outcomes Military Exposures (HOME)

Helena Chandler Director, NJ WRIISC

Office of Mental Health & Suicide Prevention

Project-1:

Enhancing Quality of Care for
GWV through Clinician Awareness
and Support

Project-2:

VET-HOME Evaluation

Project-3:

CMI-Concordant Care
and Problem-Solving
Therapy for GWI

Project-4:

Optimize Online Low
Glutamate Diet GWI
Coach



FY22 - RACGWVI Recommendations (3 OF 4)

RECOMMENDATION 3: Initiate research on the relationship between COVID-19, long-haul COVID-19, and their impact on GWI.

The long-term effects of COVID-19 on the health and quality of life for GWV already suffering from GWI are of critical interest and warrant further study. The RACGWVI recommends initiating studies on COVID-19 and persistent symptoms of long-haul COVID-19 including examining the similarities and differences between GWI and long-haul COVID-19 symptomology.

This research could utilize existing cohorts of GWV such as the Million Veteran Program (MVP) and data resources such as the COVID 19 supplemental survey or the VA Informatics and Computing Infrastructure (VINCI). The studies could yield insights into the characterization and management of both GWI and COVID-19.



2022 RACGWVI Recommendations (3 OF 4) ORD ACTION

VA RESPONSE (CONCUR).

CSP 2006: Genomics of Gulf War Illness in Veterans, was identified as key infrastructure to address research on the relationship between COVID-19, long-haul COVID-19, and their impact on GWI.

Rationale: CSP 2006 is the largest Gulf War characterized/validated cohort to date AND VA COVID Dashboard and other gold standard data sources..

- It includes 109,906 GW era veterans enrolled in the larger 49 Million Veteran Program (MVP) study cohort
 - ~41k veterans completed a GW survey of exposures, symptoms and diagnoses.
 - The CDC research case definition phenotype algorithm was applied to the CSP #2006 survey data.
 - Develop exposure variables consistent with known dates and locations of exposures.
 - 14,103 deployed, 7,463 with GWI

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2022 RACGWI Recommendations (3 OF 4) ORD ACTION

Cohort:

- GW Veterans Deployed vs Non-Deployed
- GW Veterans with and without GWI

Examples of questions:

- Assess the risk of Sars-V2 infection
- Assess the risk of COVID-19 complications (ie: medical encounters, hospitalizations)
- Assess efficacy and risk of the COVID-19 vaccine (ie: breakthrough cases, myocarditis, post-vaccine symptoms/medical encounters)
- Assess risk of long-COVID
- Assess Mortality

Action:

- Project extension/amendment was submitted by Dr. Aslan, Acting Director of CSP VA Connecticut Healthcare System and reviewed by MVP Executive Committee : May 2022
- Approved: August 2022
- IRB amended and approved
- Funded – September 2022-September 2025



2022 RACGWVI Recommendations (4 OF 4)

RECOMMENDATION 4: Continue the RACGWVI subcommittee, Veteran Engagement Sessions (VES).

A RACGWVI subcommittee, called VES, was established in January 2019 to support the Committee's mission to provide research education to GWV, to better understand the Veteran's experience of living with GWI and to build trust with the GWV community. Members of the subcommittee include the RACGWVI Chair, Designated Federal Officer, VA clinician and non-clinician researchers with expertise on chronic multi-symptom illness, GWV and other VA and non-VA subject matter experts with community leadership backgrounds. The outcomes of the VES have been highly successful. Feedback from these interactions have directly led to newly funded research projects in areas not previously examined. Additionally, participation by GWV in the VES and parent RACGWVI committee meetings have increased fivefold.

The RACGWVI recommends:

RACGWVI staff continue to work with VA and non-VA partners to facilitate maximum outreach to the 1990-91 GWV community. These communication partnerships include, but are not limited to, VA Public Affairs, VA Communications, Employee Education System (EES), War Related Illness and Injury Study Centers (WRIISC), Health Outcomes Military Exposures (HOME, formerly Post Deployment Health), Post Deployment Integrated Care Initiative (PDICI), GWV Facebook and other Veteran social media groups.

- The RACGWVI VES subcommittee resumes in person meetings twice per year as COVID-19 travel restrictions are lifted.
- The RACGWVI VES subcommittee continue to maintain a virtual meeting platform simultaneously with in-person meetings to allow nationwide attendance to continue.
- The RACGWVI VES subcommittee pinpoint rural areas as well as areas with a high population of 1990-91 GWV.
- The RACGWVI VES subcommittee support Diversity, Equity, and Inclusion (DEI) to the VES team.

VA RESPONSE (*CONCUR*). This subcommittee is already in place. Planning would involve scheduling future sessions in FY23.

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2018 RACGWVI Recommendations

Recommendation 2: Ensure that the VA is able to maximize its ongoing commitment to the deep phenotyping study of Gulf War illness (i.e., project IN-DEPTH) by taking steps in the next year that make ORD well positioned to sustain the ongoing study and further extend its research findings over the long-term.

VA Response: Concur. VA is working closely with a team including VA subject matter experts and National Institutes of Health (NIH) intramural program leaders and scientists aimed at launching a successful deep phenotyping study with the short and long-term goals of identifying the human biology of Gulf War Illnesses, with emphasis on chronic fatigue. Updated from 2017 RAC recommendations, the VA study team submitted a first draft of the VA recruitment protocol, which is under scientific review. VA will use the War Related Illness and Injury Study Center (WRIISC) sites and other VA medical centers (VAMCs) to recruit and screen Veteran participants, the clinical testing will be predominantly conducted at NIH. VA expects to collect, build, and maintain this deep phenotyping Gulf War infrastructure whereby a data- and biologics-repository are overseen by VA and made available to VA- and non-VA Gulf War investigators for validation, discovery, and targeted clinical trials.



PROJECT IN-DEPTH: VA:NIH Partnership ORD ACTION

VA NIH **I**nvestigative **D**eep **P**henotyping Study of Gulf War Veteran **H**ealth
(Project IN-DEPTH)

VA Study Co-Chairs

Nancy Klimas, MD and Matthew Reinhard, PsyD

NIH Study Team

Brian Walitt, MD and Elizabeth Bartrum





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PROJECT IN-DEPTH ORD ACTION

VA Study Team



**Study Co-Chair,
Miami FL**

N. Klimas, MD

**Study Co-Chair,
Washington DC**



M. Reinhard, PsyD



**Local Site,
East Orange NJ**

D. Helmer, MD



**Local Site,
Palo Alto CA**

W. Ashford, MD

**Local Site,
Seattle WA**



S. Hunt, MD

NIH Study PI



**NIH/NINDS,
Principal
Investigator**

B. Walitt, MD

VA ORD

**VA Gulf War
Program
Director**



K. Block, PhD



VA SHIELD

R. Bonomo, MD





PROJECT IN-DEPTH

VA Specific AIMS

VA Specific Aim 1: Gulf War (GW) Veteran recruitment, eligibility determination, and case adjudication will be applied for selection into the IN-DEPTH NIH using phone screening, comprehensive web-based assessments, medical records extractions, and in-person VA assessment.

VA Specific Aim 2: Enhance Gulf War Veteran experience and care throughout project IN-DEPTH

VA Specific Aim 3: **A)** Qualitative and Quantitative Research by VA Team. **B)** Develop a Data- and Bio-repository for future evidence-based research.

**** Enrolled and Consented 12 GWV in 2.5 months.
Exceeding expectations**



PROJECT IN-DEPTH NIH

Specific AIMS

NIH Specific Aim 1: Deep Phenotyping of GWI and Healthy Veteran Controls. We will explore the clinical and biological phenotypes of GWI, with a focus on deep measurements of basal immunologic, bioenergetic, and homeostatic regulatory parameters.

NIH Specific Aim 2: Deep Phenotyping of GWI and Healthy Veteran Controls, using methods outlined in SA1, will be performed during a peak exercise challenge. We will explore the clinical and biological phenotypes of GWI, with a focus on exercise-induced deep measurements to challenge immunologic, bioenergetic, and homeostatic regulatory parameters.

NIH Specific Aim 3: Secondary Analysis will be performed between GWI, ME/CFS, and the respective controls to explore similarities and differences in the clinical and biological phenotypes.



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Questions?